

CLAIMS

What is claimed is:

1. A method of promoting natural bypass in a mammal so provide increased blood flow to tissue served by an occluded or partly occluded vessel, comprising administering to the mammal
5 a mixture of proteins derived from ground bone.

2. The method according to claim 1 wherein the mixture of proteins derived from ground bone comprises at least two growth factors selected from the group consisting of bone morphogenic protein-2 (BMP-2), bone morphogenic protein-3 (BMP-3), bone morphogenic
10 protein-4 (BMP-4), bone morphogenic protein-5 (BMP-5), bone morphogenic protein-6 (BMP-6), bone morphogenic protein-7 (BMP-7), transforming growth factor β 1 (TGF- β 1), transforming growth factor β 2 (TGF- β 2), transforming growth factor β 3 (TGF- β 3), and fibroblast growth factor 1 (FGF-1),

15 3. The method of claim 1, wherein the mammal is a human.

4. The method of claim 1, wherein the mixture is administered subcutaneously, intramuscularly, or intravenously.

20 5. The method of claim 1, wherein the mixture is administered discretely or continuously.

6. The method of claim 1, wherein the mixture further comprises a growth factor selected from insulin-like growth factor-1 (IGF-1), epidermal growth factor (EGF), hepatocyte growth factor (HGF), transforming growth factor α (TGF- α), or platelet-derived growth factor (PDGF).

25 7. The method of claim 1, wherein the mixture further comprises a preservative or an adjuvant.

30 8. The method of claim 1, wherein the mixture comprises BMP-2, BMP-3, BMP-7, TGF- β , and FGF.

9. The method of claim 1, wherein the mixture is derived by
- (i) grinding mammalian bone, to produce ground bone;
 - (ii) cleaning the ground bone, to produce cleaned ground bone;
 - (iii) demineralizing the cleaned ground bone, to produce demineralized cleaned
 - 5 ground bone;
 - (iv) extracting protein from the demineralized cleaned ground bone using a protein denaturant; to yield extracted protein;
 - (v) ultrafiltering the extracted protein to separate out high molecular weight proteins;
 - 10 (vi) ultrafiltering the extracted protein to separate out low molecular weight proteins;
 - (vii) transferring the extracted protein to a non-ionic denaturant;
 - (viii) subjecting the extracted protein to an anion exchange process;
 - (ix) subjecting the extracted protein to a cation exchange process; and
 - 15 (x) subjecting the extracted protein to a reverse phase HPLC process.

10. The method of claim 9, wherein the mammalian bone is bovine bone.

11. A method of promoting vessel growth to heal a heart artery that has been partly or fully occluded, comprising administering to the heart a mixture of proteins derived from ground bone.

12. The method according to claim 11 wherein the mixture of proteins derived from ground bone comprises at least two growth factors selected from the group consisting of bone morphogenic protein-2 (BMP-2), bone morphogenic protein-3 (BMP-3), bone morphogenic protein-4 (BMP-4), bone morphogenic protein-5 (BMP-5), bone morphogenic protein-6 (BMP-6), bone morphogenic protein-7 (BMP-7), transforming growth factor β 1 (TGF- β 1), transforming growth factor β 2 (TGF- β 2), transforming growth factor β 3 (TGF- β 3), and fibroblast growth factor 1 (FGF-1),

13. The method of claim 11, wherein the heart is a human heart.

14. The method of claim 11, wherein the mixture is administered subcutaneously, intramuscularly, or intravenously.

15. The method of claim 11, wherein the mixture is administered discretely or continuously.

16. The method of claim 11, wherein the mixture further comprises a growth factor selected from insulin-like growth factor-1 (IGF-1), epidermal growth factor (EGF), hepatocyte growth factor (HGF), transforming growth factor α (TGF- α), or platelet-derived growth factor (PDGF).

17. The method of claim 11, wherein the mixture further comprises a preservative or an adjuvant.

18. The method of claim 11, wherein the mixture comprises BMP-2, BMP-3, BMP-7, TGF- β , and FGF.

19. The method of claim 11, wherein the mixture is derived by

- (i) grinding mammalian bone, to produce ground bone;
- (ii) cleaning the ground bone, to produce cleaned ground bone;
- (iii) demineralizing the cleaned ground bone, to produce demineralized cleaned ground bone;
- (iv) extracting protein from the demineralized cleaned ground bone using a protein denaturant; to yield extracted protein;
- (v) ultrafiltering the extracted protein to separate out high molecular weight proteins;
- (vi) ultrafiltering the extracted protein to separate out low molecular weight proteins;
- (vii) transferring the extracted protein to a non-ionic denaturant;
- (viii) subjecting the extracted protein to an anion exchange process;
- (ix) subjecting the extracted protein to a cation exchange process; and
- (x) subjecting the extracted protein to a reverse phase HPLC process.

20. The method of claim 19, wherein the mammalian bone is bovine bone.

21. A method of promoting angiogenesis to assist in recovery from tissue damage,
5 comprising administering to the tissue a mixture of proteins derived from ground bone.

22. The method according to claim 21 wherein the mixture of proteins derived from ground
bone comprises at least two growth factors selected from the group consisting of bone
morphogenic protein-2 (BMP-2), bone morphogenic protein-3 (BMP-3), bone morphogenic
10 protein-4 (BMP-4), bone morphogenic protein-5 (BMP-5), bone morphogenic protein-6 (BMP-
6), bone morphogenic protein-7 (BMP-7), transforming growth factor β 1 (TGF- β 1),
transforming growth factor β 2 (TGF- β 2), transforming growth factor β 3 (TGF- β 3), and
fibroblast growth factor 1 (FGF-1),

15 23. The method of claim 21, wherein the tissue is human tissue.

24. The method of claim 21, wherein the mixture is administered subcutaneously,
intramuscularly, or intravenously.

20 25. The method of claim 21, wherein the mixture is administered discretely or continuously.

26. The method of claim 21, wherein the mixture further comprises a growth factor selected
from insulin-like growth factor-1 (IGF-1), epidermal growth factor (EGF), hepatocyte growth
factor (HGF), transforming growth factor α (TGF- α), or platelet-derived growth factor (PDGF).

25 27. The method of claim 21, wherein the mixture further comprises a preservative or an
adjuvant.

28. The method of claim 21, wherein the mixture comprises BMP-2, BMP-3, BMP-7, TGF-
30 β , and FGF.

29. The method of claim 21, wherein the mixture is derived by
- (i) grinding mammalian bone, to produce ground bone;
 - (ii) cleaning the ground bone, to produce cleaned ground bone;
 - (iii) demineralizing the cleaned ground bone, to produce demineralized cleaned
- 5 ground bone;
- (iv) extracting protein from the demineralized cleaned ground bone using a protein denaturant; to yield extracted protein;
 - (v) ultrafiltering the extracted protein to separate out high molecular weight
- 10 proteins;
- (vi) ultrafiltering the extracted protein to separate out low molecular weight
- proteins;
- (vii) transferring the extracted protein to a non-ionic denaturant;
 - (viii) subjecting the extracted protein to an anion exchange process;
 - (ix) subjecting the extracted protein to a cation exchange process; and
 - (x) subjecting the extracted protein to a reverse phase HPLC process.
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30. The method of claim 29, wherein the mammalian bone is bovine bone.